UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/444,790	05/19/1995	MANFRED BROCKHAUS	9189	5612

37500 7590 03/07/2011

AMGEN INC.
LAW DEPARTMENT
1201 AMGEN COURT WEST
SEATTLE, WA 98119

EXAMINER	
HOWARD, ZACHARY C	
ART UNIT	PAPER NUMBER
1646	

MAIL DATE	DELIVERY MODE
03/07/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	08/444,790	BROCKHAUS ET AL.	
	Examiner	Art Unit	
	ZACHARY C. HOWARD	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 December 2010*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *62,102,103,105-107,110,111,113,114,119-121,123-137 and 140-148* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *62,102,103,105-107,110,111,113,114,119-121,123-137 and 140-148* is/are rejected.

7)☒ Claim(s) *110,111,113,114,123,124,132,133,137,141,142 and 144-148* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 May 1995* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/16/10; 12/16/10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

Applicants filed an appeal to the Board of Patent Appeals and Interferences regarding the following rejections made final in the 2/23/07 Office Action:

The rejection of claims 62, 102, 103, 105-107, 110, 111, 113, 114, 119-121 and 123-137 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement.

The rejection of claims 62, 102, 103, 105-107, 110, 111, 113, 114, 119-121, 125-131 and 134-137 under 35 U.S.C. 103(a) as being unpatentable over Dembic et al (1990) in view of Capon et al (U.S. 5,116,964).

The rejection of claims 140-144 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement because the claims contain new matter.

In the 11/22/10 Board decision, each of the above rejections was reversed.

In view of the new grounds of rejection set forth below, PROSECUTION IS HEREBY REOPENED.

The amendment of 12/16/10 has been entered in full. Claim 139 is canceled. New claims 145-148 are added.

The 12/16/10 claim listing contains non-compliant markings to three claims having the status identifier of "Previously Presented". Claim 106, line 3, has a marking indicating a space is inserted between the words "TNF" and "receptor". However, this space was present previously (see claim 106 in the 11/14/06 claim listing). Claim 107, line 5, has a marking indicating that the word "a" is deleted. However, this word was deleted previously (see claim 107 in the 10/6/06 claim listing). Claim 111, line 1, has a marking indicating a comma was added. However, this comma was added previously (see claim 111 in the 12/14/05 claim listing). Furthermore, claim 141 is missing a status identifier, which should be "(Previously Presented)". The 12/16/10 claims have been

entered despite these non-compliant markings. Applicants should remove all markings indicating previously entered changes from any future claim listing(s).

In view of the cancellation of claim 139, the restriction requirement between the elected invention and the invention of claim 139, set forth at pg 2 of 2/23/07 Office Action, is currently moot, but will be reinstated if any new claims to the invention of claim 139 are added in subsequent claim amendments.

Claims 62, 102, 103, 105-107, 110, 111, 113, 114, 119-121, 123-137 and 140-148 are pending in the instant application.

Information Disclosure Statement

The two Information Disclosure Statements filed on 12/16/10 have each been considered.

Claim Objections

Claims 110, 111, 113, 114, 123, 124, 132, 133, 137, 141, 142 and 144-148 are objected to because of the following informalities:

(1) In each of claims 110, 111, 113 and 132, the preamble of the claim should recite "The recombinant protein" rather than just "The protein". Parent claim 107 uses the term "A recombinant protein" and dependent claims 128-131 refer to the "The recombinant protein of claim 107". For clarity, all claims depending from claim 107 should refer to the protein of claim 107 in the same manner.

(2) Claim 114 is objected to for referring to the "recombinant protein of claims 62, 107, 134 or 135" but parent claims 62, 134 and 135 use the term "A protein" rather than "A recombinant protein".

(3) In each of claims 123, 124, 132 and 133, the term "pCD4Hγ1" should be written as "pCD4-Hγ1" (i.e., hyphenated), as in the specification at page 17, line 26. Also, compare with the term "pCD4-Hγ3", which is hyphenated in claims 123 and 132.

(4) Claims 137, 146 and 148 are objected to for referring to the "recombinant protein of claim …" but parent claims 105, 146 and 148 use the term "The protein" rather than "The recombinant protein".

(5) Claims 141, 142, and 144 should have a comma after the phrase "claim 140" or "claim 142" (compare with the other dependent claims, such as claim 143).

(6) In each of claims 145 and 147, the term "IgG1" should be written as "IgG_1", as in claims 105, 106, 113, 131 and 134.

Appropriate correction is required.

Claim Rejections - 35 USC § 112, 4th paragraph

The following is a quotation of the fourth paragraph of 35 U.S.C. 112:

> Subject to the following paragraph, a claim in dependent form shall contain a reference to a claim previously set forth and then specify a further limitation of the subject matter claimed. A claim in dependent form shall be construed to incorporate by reference all the limitations of the claim to which it refers.

Claim 111 is rejected under 35 U.S.C. 112, fourth paragraph, as being of improper dependent form for failing to further limit the subject matter of a previous claim.

See the "Supplementary Examination Guidelines for Determining Compliance With 35 U.S.C. 112 and for Treatment of Related Issues in Patent Applications" (Federal Register, Vol. 76, No. 27, Wednesday, February 9, 2011), pg 7166, section "5. Dependent Claims", which states that "If the dependent claim does not comply the with the requirements of § 112, ¶4, the examiner should reject the dependent claim under § 112, ¶4 as unpatentable rather than objecting to the claim" and "a dependent claim must be rejected under § 112, ¶4 if it omits an element from the claim upon which it depends or it fails to add a limitation to the claim upon which it depends".

Specifically, dependent claim 111 recites "The protein of claim 110, wherein the soluble fragment further comprises the peptide LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10). Claim 110 in turn depends from independent claim 107. However, claim 107 already limits the soluble fragment of the protein to that comprises SEQ ID NO: 10. See lines 5-6, which state that "said soluble fragment comprising the amino acid sequence LPAQVAFXPYAPEPGSTC (SEQ ID NO: 10)".

Therefore, dependent claim 111 is of improper dependent form because it fails to further limit the subject matter of parent claims 107 and 110.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 62, 102, 103, 105-107, 110, 111, 113, 114, 119-121, 123-137 and 140-148 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent 5,395,760 (Smith et al; published 3/7/1995, filed 5/10/1990), and further in view of U.S. Patent 5,428,130 (Capon et al; reference A64 on the 1/22/07 IDS).

Claims 62, 102, 103, 105-107, 110, 111, 113, 119-121, 125-131, 134-136 and 145 each encompass the following protein: a purified protein recombinantly produced in CHO cells, which specifically binds human tumor necrosis factor (TNF) and consists of the following parts (a) and (b):

Part (a) of each claim encompasses a TNF-binding soluble fragment including SEQ ID NO: 10, 8 and 12 of an insoluble human TNF receptor, wherein said receptor has three characteristics: (i) specifically binds human TNF; (ii) molecular weight of about 75 kD; and (iii) comprises SEQ ID NO: 10, 8, 12, 13 and 9.

Part (b) of each claim encompasses “all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant

region". The narrowest claims limit the immunoglobulin heavy chain to human IgG_1; however, each of the claims encompasses this limitation.

Smith et al teach the amino acid sequence of a human TNF receptor in Figure 2A-2B. This receptor sequence includes instant SEQ ID NO: 10 (amino acid residues 8-18 of Figure 2A-2B), SEQ ID NO: 8 (residues 43-47), SEQ ID NO: 12 (residues 114-117), SEQ ID NO: 13 (residues 278-284) and SEQ ID NO: 9 (residues 324-339), and also includes a transmembrane domain (residues 235-265) that renders the receptor "insoluble" as used in the instant claims. Smith et al teach that the sequence has an "apparent molecular weight by SDS-PAGE of about 80 kilodaltons (kDa)" (col 3, lines 47-49), which is encompassed by the recitation of "about 75 kilodaltons on a non-reducing SDS-polyacrylamide gel" in the instant claims. Thus, Smith et al teach an insoluble human TNF receptor with limitations (i)-(iii) as recited in the claims.

Smith et al further teach that the invention includes "Soluble TNF-R" corresponding to all of the extracellular region of a native TNF-R, including amino acids 1-235 of Figure 2A, "and which are biologically active in that they bind to TNF ligand" (col 4, lines 12-21). Thus, Smith et al teach a human TNF-binding soluble fragment of an insoluble human TNF receptor as encompassed by part (a) of the instant claims.

Smith et al also include a section titled "Proteins and Analogs" (starting at col 7, line 8), which includes the following teachings:

> Subunits of TNF-R may be constructed by deleting terminal or internal residues or sequences. Particularly preferred sequences include those in which the transmembrane region and intracellular domain of TNF-R are deleted or substituted with hydrophilic residues to facilitate secretion of the receptor into the cell culture medium. The resulting protein is referred to as a soluble TNF-R molecule which retains its ability to bind TNF. A particularly preferred soluble TNF-R construct is TNF-RΔ235 (the sequence of amino acids 1-235 of FIG. 2A), which comprises the entire extracellular region of TNF-R, terminating with Asp^{235} immediately adjacent the transmembrane region. (col 9, lines 17-29)
>
> Both monovalent forms and polyvalent forms of TNF-R are useful in the compositions and methods of this invention. Polyvalent forms possess multiple TNF-R binding sites for TNF ligand. For example, a bivalent soluble TNF-R may consist of two tandem repeats of amino acids 1-235 of FIG. 2A, separated by a linker region. Alternate polyvalent forms may also be constructed, for example, by chemically coupling TNF-R to any clinically acceptable carrier

> molecule, a polymer selected from the group consisting of Ficoll, polyethylene glycol or dextran using conventional coupling techniques. (col 9, lines 33-44).
>
> A recombinant chimeric antibody molecule may also be produced having TNF-R sequences substituted for the variable domains of either or both of the immunoglobulin molecule heavy and light chains and having unmodified constant region domains. For example, chimeric TNF-R/IgG_1 may be produced from two chimeric genes--a TNF-R/human κ light chain chimera (TNF-R/C_κ) and a TNF-R/human γ1 heavy chain chimera (TNF-R/$C_{\gamma\text{-}1}$). Following transcription and translation of the two chimeric genes, the gene products assemble into a single chimeric antibody molecule having TNF-R displayed bivalently. Such polyvalent forms of TNF-R may have enhanced binding affinity for TNF ligand. Additional details relating to the construction of such chimeric antibody molecules are disclosed in WO 89/09622 and EP 315062 (col 9, lines 53-68).

Thus, Smith et al teach proteins that fuse TNF-R sequences, including the soluble extracellular domain, and the unmodified constant regions of either or both of the heavy and light chains of human IgG_1. In each case (i.e., when either or both of the heavy and light chains is substituted), the TNF-R sequence is substituted for a variable domain, which is found on each of the heavy and light chains. Thus, by teaching substitutions for "either or both of the heavy and light chains of human IgG_1", Smith et al teach fusion proteins in which the heavy chain variable domains are substituted with the TNFR sequences, or the light chain variable domains are substituted with the TNFR sequences, or both. Due to disulfide bonding between the heavy chains and light chains, the resultant fusion proteins would form a tetrameric structure (two heavy chains and two light chains), but with either two or four TNF-binding sites, depending on whether the TNFR extracellular domains are substituted for the heavy chain variable domains (two binding sites), the light chain variable domains (two binding sites) or both (four binding sites).

Smith et al further teach administration of soluble TNF-R proteins of the invention (col 16, line 57 to col 17, line 27). Smith et al also teach that "TNF-R derivatives can be used as immunogens, reagents in receptor-based immunoassays, or as binding agents for affinity purification procedures of TNF or other binding ligands" (col 8, lines 1-4). Smith et al further teach that "TNF-R protein fusions can comprise peptides added to facilitate purification or identification of TNF-R (e.g., poly-His)" (col 7, lines 54-56).

Smith et al do not teach fusion proteins between the extracellular domain of the TNF-R and immunoglobulin sequences wherein the constant region of the heavy chain of human IgG_1 has all of the domains other than the first domain (i.e., is missing the first domain of the constant region).

Capon et al teach hybrid immunoglobulins comprising the extracellular domain of a membrane bound receptor, both generally and with a specific example (Example 4, starting in column 40) wherein truncated murine lymphocyte homing receptor (MHLR) extracellular domain is fused to the Fc region of human IgG_1 ("These truncated proteins are all joined to a human heavy chain γ 1 region just upstream of the hinge domain (H) such that these chimeras contains the two cysteine residues of the hinge responsible for dimerization as well as the CH2 and CH3 constant regions"). Capon et al further teach that the "ligand binding partner" can be any portion of a receptor that retains ligand binding (col 7, lines 15-35). Capon et al further teach a variety of structures for the molecules, including both homodimers (col 9, lines 63-68) and different configurations of tetramers (col 11, lines 1-35). Capon et al teach that the "A" in the homotetramer structure shown in column 11 can be the same or different (see col 10, lines 57-59). Thus, the homotetramer structure shown in column 11 encompasses each of the immunoglobulin fusion proteins taught by Smith et al (described above).

Capon et al further teach that "a particularly preferred embodiment is a fusion of an N-terminal portion of a LHR, which contains the binding site for the endothelium of lymphoid tissue, to the C-terminal Fc portion of an antibody, containing the effector functions of immunoglobulin G_1. There are two preferred embodiments of this sort; in one, the entire heavy chain constant region is fused to a portion of the LHR; in another, a sequence beginning in the hinge region just upstream of the papain cleavage site which defines IgG Fc chemically (residue 216, taking the first residue of heavy chain constant region to be 114 … is fused to a portion of the LHR. The latter embodiment is described in the Example 4" (col 15, lines 4-18). The Fc portion of an antibody includes the CH2 and CH3 domains of the constant region but does not include the CH1 domain. Capon et al further teach in Example 4 that "junctional sites between the LHR and human IgG sequences was chosen such that the Joining of the molecules near the

hinge region resulted in chimeric molecules that were efficiently synthesized and dimerized in the absence of any light chain production" (col 40, lines 50-55).

Capon et al further teach recombinant production of hybrid immunoglobulins in cell culture (column 26, lines 24-26). Capon et al further teach that CHO cells are suitable eukaryotic cells for production of hybrid immunoglobulins (column 29, line 37). Capon et al further teach purification of the hybrid immunoglobulin from cell cultures following expression in host cells (column 30, line 26-27).

Capon et al further teach a variety of uses for fusion proteins of the invention, including prolonging in vivo plasma half-life, facilitating purification, for therapeutic uses, or diagnostic reagents for in vitro assay of ligand binding partners (col 4, lines 40-59). Capon et al provide further teachings regarding use of the fusion proteins for purification of the "ligand binding partner": "The novel polypeptide of this invention are useful in diagnostics or in purification of the ligand binding partner by immunoaffinity techniques known per se. Alternatively, in the purification of the binding partner, the novel polypeptides are used to adsorb the fusion from impure admixtures, after which the fusion is eluted and, if desired, the binding partner is recovered from the fusion, e.g., by enzymatic cleavage" (column 17, lines 54-61).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to create the claimed protein by substituting a human IgG_1 heavy chain comprising all of the domains of the constant region other than the first domain as taught by Capon et al for the unmodified human IgG_1 heavy chain constant region in a fusion protein taught by Smith et al. The person of ordinary skill in the art would be motivated to make said substitution because (1) Capon et al teach the modified heavy chain constant region lacking the first domain of the constant region as an alternate preferred embodiment for use in constructing fusion proteins between ligand binding portions of receptor and immunoglobulin proteins, and (2) making such a substitution would obviate the need for co-expression of immunoglobulin light chains, resulting in a simpler system requiring expression of a single component. The person of ordinary skill in the art would use the resultant fusion protein for (1) any of TNF-binding uses taught by Smith et al; or (2) for purification of the TNF-R sequences, as Smith et al teach that

fusion proteins can be used for TNF-R purification, and Capon et al teach that immunoglobulin fusion proteins can be used for ligand binding partner purification.

The person of ordinary skill in the art would have had a reasonable expectation of success in making said substitution because it would only require a simple substitution of one known element for use in immunoglobulin fusion protein for another known element to obtain predictable results. The teachings of Smith et al include TNF-R-immunoglobulin fusion proteins in which the variable region of only the heavy chain is substituted with TNF-binding sequences from TNF-R, which results in production of a tetrameric molecule with only two TNF binding sites. A substitution for the heavy chain molecule taught by Capon et al would also produce a molecule with two TNF-binding sites. The difference would be that the lack of the first constant region domain would result in the lack of inclusion of an immunoglobulin light chain in the final molecule. The skilled artisan would expect the resultant fusion protein to be produced and function in the absence of light chain in view of the teachings of the teachings of Capon et al in Example 4 that the fusion proteins were synthesized and dimerized in the absence of light chain production.

As described above, Smith et al also teach that bivalent forms of soluble TNF-R may consist of two tandem repeats of amino acids 1-235 of FIG.2A, separated by a linker. The skilled artisan at the time of filing would recognize the Fc region as taught by Capon et al as qualifying as such a linker region, thus providing further support for a reasonable expectation of success.

Claims 123, 124, 132 and 133 depend, respectively, from claims 62, 105, 107 and 113, and encompass a protein of the parent claim wherein the domains of the constant region of the human immunoglobulin heavy chain consist essentially of the immunoglobulin sequence encoded by pCD4Hγ1 vector (deposited at Deutschen Sammlung von Mikroorganismen unde Zellkulturen GmbH (DSM) in Braunchsweig, FRG under No. DSM 5314). The specification teaches that the pCD4Hγ1 is described in detail in European Patent Application No. 90107393.2, which was published as EP 394827 (reference B42 on the 1/22/07 IDS). The '827 publication teaches that the

pCD4Hγ1 plasmid contains a sequence encoding the "Hinge and the C2 and C3 constant region" of "human Igγ1 heavy chain" (pg 7). Therefore, claims 123, 124, 132 and 133 each encompass a protein in which the domains of the constant region of the human immunoglobulin heavy chain consist essentially of the Hinge and the C2 and C3 constant region of human Igγ1 (IgG1) heavy chain. This is the same embodiment used to rejection claims 62, 105, 107 and 113 above. Therefore, claims 123, 124, 132 and 133 are included in the rejection for the same reasons as described above for claims 62, 105, 107 and 113.

Claims 140-144 and 147 each encompass the following protein: a protein recombinantly produced in CHO cells that specifically binds human TNF and consists of parts (a) and (b).

Part (a) of each claim encompasses a human TNF-binding soluble fragment of the amino acid sequence encoded by cDNA insert of the plasmid deposited with the ATCC on October 17, 2006 under the accession number PTA 7942.

Part (b) of each claim encompasses "all of the domains of the constant region of a human immunoglobulin IgG heavy chain other than the first domain of said constant region".

The specification (as amended on 11/14/06) at page 10, line 34, indicates that ATCC deposit number PTA 7942 contains DNA sequences that encode for an insoluble TNF-binding protein. The third declaration of Dr. Werner Lesslauer under 35 U.S.C. 1.132 filed on 11/14/06 states that the ATCC deposit number PTA 7942 is a DNA construct containing the extracellular region of human p75 tumor necrosis factor receptor (TNFR). Thus, the evidence indicates that the soluble fragment of the cDNA insert of ATCC deposit number PTA 7942 is the same extracellular region as taught by Smith et al for the 80 kD TNF receptor (i.e., amino acid residues 1-235 of Figure 2A-2B of Smith et al). Therefore, claims 140-144 and 147 are included in the rejection for the same reasons as described above for claims 62, 102, 103, 105-107, 110, 111, 113, 119-121, 125-131, 134-137, 145 and 146,

With respect to claims 114, 137, 146 and 148, the recitation of “a pharmaceutical composition” in the preamble of the claim is interpreted as an intended use and bears no accorded patentable weight. Therefore, the claims encompass any composition comprising a recombinant protein of claims 62, 107, 134 or 135 (claim 114), claim 105 (claim 137), claim 145 (claim 146), or claim 147 (claim 148) and a pharmaceutically acceptable carrier material.

Smith et al further teach administration of soluble TNF-R proteins of the invention, and that for such uses, soluble TNF-R proteins of the invention can be placed in compositions comprising purified protein in conjunction with physiologically acceptable carriers, excipients or diluents (col 16, line 57 to col 17, line 27). Smith et al also teach that "TNF-R derivatives can be used as immunogens, reagents in receptor-based immunoassays, or as binding agents for affinity purification procedures of TNF or other binding ligands" (col 8, lines 1-4).

Capon et al further teach placement of the purified hybrid immunoglobulin in “sterile, isotonic formulations” that are “preferably liquid” and “ordinarily a physiologic salt solution” (column 31, lines 4-8). Such solutions meet the definition of a “pharmaceutically acceptable carrier material” (as in claim 114). Capon et al further teach a variety of uses for fusion proteins of the invention, including prolonging in vivo plasma half-life, facilitating purification, for therapeutic uses, or diagnostic reagents for in vitro assay of ligand binding partners (col 4, lines 40-59). Capon et al alternately teach that the fusion proteins can also be used to simply purify the ligand bind partner itself (col 17).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to further include the hybrid TNF-R-immunoglobulin described above that is obvious over Smith et al in view of Capon et al in a composition with a pharmaceutically acceptable carrier material. The person of ordinary skill in the art would be motivated to do so in order to resuspend the hybrid immunoglobulin following purification as taught by Capon et al, for any use taught by Smith et al or Capon et al. Resuspending the protein in a composition comprising a pharmaceutically acceptable carrier would allow the composition to retain versatility in any of the uses taught by

Smith et al or Capon et al (i.e., purification or administration). The person of ordinary skill in the art would have expected success because Capon et al teach the necessary procedures for purification and resuspension of the hybrid immunoglobulin, and both references teach pharmaceutically acceptable carriers.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachary C. Howard whose telephone number is 571-272-2877. The examiner can normally be reached on M-F 9:30 AM - 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary B. Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Z. C. H./
Examiner, Art Unit 1646

/Gary B. Nickol /
Supervisory Patent Examiner, Art Unit 1646

/George C. Elliott/
Director, Technology Center 1600